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US DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

ATTORNEY DOCKET NUMBER  
2001-0662AU.S. APPLICATION NO.  
**09/857416**  
(if known, see 37 CFR 1.57)  
[NEW]TRANSMITTAL LETTER TO THE UNITED STATES  
DESIGNATED/ELECTED OFFICE (DO/EO/US)  
CONCERNING A FILING UNDER 35 U.S.C. §371International Application No.  
PCT/EP99/09517International Filing Date  
December 6, 1999Priority Date Claimed  
December 28, 1998

## Title of Invention

PROCESS FOR PREPARING GLYOXYLIC ESTERS OR THEIR HYDRATES

## Applicant(s) For DO/EO/US

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Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1.  This is a **FIRST** submission of items concerning a filing under 35 U.S.C. §371.
2.  This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. §371.
3.  This express request to begin national examination procedures (35 U.S.C. §371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. §371(b) and PCT Articles 22 and 39(1).
4.  A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5.  A copy of the International Application as filed (35 U.S.C. §371(c)(2))
  - a.  is transmitted herewith (required only if not transmitted by the International Bureau).
  - b.  has been transmitted by the International Bureau.
  - c.  is not required, as the application was filed in the United States Receiving Office (RO/US)
6.  A translation of the International Application into English (35 U.S.C. §371(c)(2)). **ATTACHMENT A**
7.  Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. §371(c)(3)).
  - a.  are transmitted herewith (required only if not transmitted by the International Bureau).
  - b.  have been transmitted by the International Bureau.
  - c.  have not been made; however, the time limit for making such amendments has NOT expired.
  - d.  have not been made and will not be made.
8.  A translation of the amendments to the claims under PCT Article 19.
9.  An oath or declaration of the inventor(s) (35 U.S.C. §371(c)(4)). **ATTACHMENT B**
10.  A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. §371(c)(5)).

## Items 11. to 14. below concern other document(s) or information included:

11.  An Information Disclosure Statement under 37 CFR 1.97 and 1.98. **ATTACHMENT C**
12.  An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.  
**ATTACHMENT D**
13.  A **FIRST** preliminary amendment.  
 A **SECOND** or **SUBSEQUENT** preliminary amendment.
14.  Other items or information:
  - a. Cover Page of Published International Application No. WO 00/39068 - **ATTACHMENT E**
  - b. International Search Report - **ATTACHMENT F**

U.S. APPLICATION NO. [NEW] <b>09/857416</b>	INTERNATIONAL APPLICATION NO. PCT EP99/09517	ATTORNEY'S DOCKET NO. 2001-0662A	
15. [X] The following fees are submitted		<b>CALCULATIONS</b>	
<b>BASIC NATIONAL FEE (37 CFR 1.492(a)(1)-(5)):</b>			
Neither international preliminary examination fee nor international search fee paid to USPTO and International Search Report not prepared by the EPO or JPO .....		\$1000.00	
International Search Report has been prepared by the EPO or JPO .....		\$ 860.00	
International preliminary examination fee not paid at USPTO but international search paid to USPTO .....		\$ 710.00	
International preliminary examination fee paid to USPTO but claims did not satisfy provisions of PCT Article 33(1)-(4) .....		\$ 690.00	
International preliminary examination fee paid at USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) .....		\$ 100.00	
<b>ENTER APPROPRIATE BASIC FEE AMOUNT =</b>		\$860.00	
Surcharge of \$130.00 for furnishing the oath or declaration later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(e)).			
Claims	Number Filed	Number Extra	Rate
Total Claims	9 -20 =	0	X \$18.00
Independent Claims	1 - 3 =	0	X \$80.00
Multiple dependent claim(s) (if applicable)		+ \$270.00	
<b>TOTAL OF ABOVE CALCULATIONS =</b>		\$860.00	
[ ] Small Entity Status is hereby asserted. Above fees are reduced by 1/2.			
<b>SUBTOTAL =</b>		\$860.00	
Processing fee of \$130.00 for furnishing the English translation later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(f)).		+ \$130.00	
<b>TOTAL NATIONAL FEE =</b>		\$860.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40 per property + \$ 40.00			
<b>TOTAL FEES ENCLOSED =</b>		\$900.00	
		Amount to be refunded \$	
		Amount to be charged \$	
<p>a. [X] A check in the amount of <u>\$ 900.00</u> to cover the above fees is enclosed. A duplicate copy of this form is enclosed.</p> <p>b. [ ] Please charge my Deposit Account No. 23-0975 in the amount of \$ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.</p> <p>c. [X] The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. <u>23-0975</u>.</p>			
<p><b>NOTE:</b> Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.</p>			
19. CORRESPONDENCE ADDRESS		<p>By: <u>Matthew Jacob</u>            Matthew Jacob,            Registration No. 25,154</p> <p>WENDEROTH, LIND &amp; PONACK, L.L.P.            2033 "K" Street, N.W., Suite 800            Washington, D.C. 20006-1021            Phone:(202) 721-8200            Fax:(202) 721-8250</p> <p>June 4, 2001</p>	
<p>[CHECK NO.] <u>WU772</u></p> <p>[2001-0662A]</p>			

Process for preparing glyoxylic esters or their hydrates

Glyoxylic esters, for example ethyl glyoxylate,  
5 methyl glyoxylate, benzyl glyoxylate or L-(-)-menthyl  
glyoxylate, are important reagents in organic  
chemistry, since the  $\alpha$ -oxo ester group is a highly  
reactive group which can take part in a number of  
reactions. L-(-)-Menthyl glyoxylate (MGH) is, for  
10 example, an important C<sub>2</sub> building block for asymmetric  
synthesis, for chiral acetals, for oxathiolanes, for  
stereo-controlled addition reactions to alkenes and  
nitroalkanes, or for Grignard reactions.

The preparation of glyoxylic esters from the  
15 corresponding maleic or fumaric diesters by means of a  
two-stage ozonolysis and reduction process is already  
known from a number of literature references.

Thus, for example, according to J. Org. Chem.  
1982, 47, pp. 891-892 ethyl, methyl or benzyl  
20 glyoxylates are obtained by ozonolysis of the  
corresponding maleic diesters in dichloromethane,  
subsequent reduction of the ozonide by means of  
dimethyl sulfide and subsequent distillation.

WO 96/22960 also describes a two-stage process  
25 for preparing menthyl glyoxylate as intermediate for  
menthyl dihydroxyacetate, in which dimenthyl maleate or  
dimenthyl fumarate is ozonized in the first stage in a  
halogenated hydrocarbon or carboxylic ester, preferably  
in the presence of a lower aliphatic alcohol, and in  
30 the second stage the resultant ozonolysis product is  
either reduced with a dialkyl sulfide or by catalytic  
hydrogenation with hydrogen to give menthyl glyoxylate.

The disadvantage with the previously known  
processes, however, is that after the ozonolysis step,  
35 peroxide-containing ozonolysis products are present,  
which must then be reduced in a second step, either by  
means of catalytic hydrogenation or in the presence of  
dialkyl sulfides or aryl sulfides, trialkyl phosphides,  
to give the corresponding glyoxylic esters.

To avoid these problems, EP 0 884 232 A1 proposed, for example, preparing MGH via ozonolysis of maleic acid monomenthyl ester sodium salt as starting material. Although in this process the previously necessary reduction step is omitted, the starting material used is not available on the market and must therefore be prepared in an additional stage by reacting maleic anhydride with menthol.

DE 44 35 647 further discloses a process in which a 50% strength glyoxylic acid solution is esterified with an excess of menthol using sulfuric acid and azeotropic removal of water. The monohydrate of MGH is isolated from the reaction mixture by forming a bisulfite adduct and phase separation with subsequent release from the adduct.

The disadvantage of this process is the complex isolation, the necessity of very gentle drying of the product, and the considerable amount of waste.

Tetrahedron Lett. 39, 4223-4226 (1998) discloses the transesterification of ethyl glyoxylate diethyl acetal with titanium(IV) ethoxide. However, in this reaction, first, an expensive starting material is used, and secondly, the described workup of the reaction mixture after the reaction mixture has ended, by hydrolysis of the catalyst and flash chromatography, is problematic and too expensive for an industrial scale.

It was therefore an object of the present invention to find a process for preparing glyoxylic esters which does not have the abovementioned disadvantages of previously known processes.

The present invention therefore relates to a process for preparing glyoxylic esters which comprises  
a) transesterifying a glyoxylic ester hemiacetal directly with an alcohol in the presence of a catalyst, or  
b) first converting a glyoxylic ester hemiacetal into the corresponding glyoxylic ester acetal and then

transesterifying it with an alcohol in the presence of a catalyst,

whereupon, following a) and b, the acetal is cleaved to give the desired free glyoxylic ester or its hydrate.

5 According to the invention the starting material used is a glyoxylic ester hemiacetal. Suitable glyoxylic ester hemiacetals are described, for example, in EP-P-0 099 981.

10 Preference is given to glyoxylic acid methyl ester methyl hemiacetal (GMHA), glyoxylic acid ethyl ester hemiacetals, glyoxylic acid propyl ester hemiacetals, glyoxylic acid isopropyl ester hemiacetals, glyoxylic acid t- or n-butyl ester hemiacetals.

15 Particularly preferably, GMHA is used as starting compound.

Glyoxylic esters or their hydrates which are obtained by the inventive process are compounds whose ester moiety is derived either from chiral or nonchiral primary, secondary or tertiary alcohols. Esters of 20 primary alcohols are preferably derived from ethanol, butanol, propanol and hexanol. Preferably, esters of secondary or tertiary alcohols, in particular acyclic, monocyclic, bicyclic terpene alcohols, or of acyclic, 25 monocyclic, tricyclic sesquiterpene alcohols, di- or triterpene alcohols are prepared, which may be unsubstituted or substituted.

Particularly preferred end products are glyoxylic esters or their hydrates which are derived from optionally variously substituted monocyclic or 30 bicyclic terpene alcohols, for instance from menthols, phenylmenthol, borneol, fenchol, etc.

In the inventive process, the hemiacetal can be transesterified either directly (variant a) to give the desired glyoxylic ester, or it can first be converted 35 into the corresponding acetal (variant b), which is then transesterified in a similar manner to variant a).

The hemiacetal is converted into the corresponding acetal in a manner known per se by means of an alcohol and acid catalysis.

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The acetalization is preferably performed using the alcohol which is already present in the hemiacetal. However, it is also possible to prepare mixed acetals. Suitable alcohols are methanol, ethanol, propanol, 5 butanol, hexanol. Preferably, the hemiacetals are therefore converted into glyoxylic acid ester dimethyl acetals, diethyl acetals, etc. Particular preference is given to glyoxylic acid methyl ester dimethyl acetal.

The corresponding alcohol is used either in the 10 liquid stage or vapor stage for the acetalization. Preferably, the acetalization is carried out using alcohol vapor.

Suitable catalysts are customary acids, such as H<sub>2</sub>SO<sub>4</sub>, p-toluenesulfonic acid, acid ion exchangers, etc. 15 Preferably, H<sub>2</sub>SO<sub>4</sub> is used.

The water eliminated is preferably discharged together with the superheated alcohol vapor and is thus continuously taken off from the reaction mixture. The transesterification of the hemiacetals or acetals 20 is performed in an alcohol as reaction medium. Preferably, anhydrous alcohols are used.

To obtain the above-described glyoxylic esters, therefore the alcohol is used which leads to the desired ester moiety in the end product. 25 These are accordingly chiral or nonchiral, primary, secondary or tertiary alcohols, preferably secondary or tertiary alcohols, in particular acyclic, monocyclic, bicyclic terpene alcohols, monocyclic or tricyclic, sesquiterpene alcohols, di- or triterpene alcohols. 30 Particularly preferred alcohols are therefore again optionally variously substituted mono- or bicyclic terpene alcohols, for example menthols, phenylmethols, borneol, fenchol, etc.

The corresponding alcohol can be used in an 35 equimolar amount, but also either in excess or in a deficiency.

Thus, it is preferred, in the case of cheaper alcohols, to add these in excess to the hemiacetal or acetal,

whereas in the case of expensive alcohols, for instance menthol etc., the acetal is used in excess.

In addition to the alcohol used, a further anhydrous solvent can be used, for instance 5 unsubstituted or substituted C<sub>5</sub>-C<sub>20</sub>alkanes, for example hexane and heptane etc., and alkenes, silicon compounds, for instance silicone oil etc., or other solvents which are inert under the reaction conditions.

The transesterification takes place according 10 to the invention in the presence of specific catalysts. Catalysts which come into consideration are stannic, titanic or zirconic esters, lithium compounds, and basic catalysts.

Suitable catalysts, from the group of the tin 15 catalysts, are dialkyltin dicarboxylates having 1-12 carbon atoms in the alkyl moiety. Dicarboxylate moieties which come into consideration are diacetates, dilaurates, maleates, diisooctanates, or mixed dicarboxylates, in particular with longer-chain fatty 20 acid esters.

Examples of these are dibutyltin diacetate, dibutyltin dilaurate, dibutyltin diisooctoate, dibutyltin maleate, dioctyltin dilaurate, etc.

Preferably dibutyltin diacetate, mixed dibutyltin 25 dicarboxylates with longer-chain fatty esters and dioctyltin dilaurate are used.

Suitable titanium catalysts are titanium(IV) ethoxide, isopropoxide, propoxide, butoxide, isobutoxide, etc.

30 Preferably, titanium(IV) isopropoxide is used.

Suitable catalysts from the group of zirconium catalysts are zirconates, such as tetrapropyl zirconate, tetraisopropyl zirconate, tetrabutyl zirconate, citric acid diethyl ester zirconate, etc.

35 Lithium catalysts which can be used are lithium salts, for example chlorides, lithium alkoxides or lithium hydroxides, but also organic lithium compounds, for

instance butyllithium. A preferred lithium catalyst is butyllithium.

However, in particular in the case of variant b), basic catalysts can also be used, for instance alkali metal 5 (Na,K) compounds, alkaline earth metal (Mg) compounds or aluminum compounds. Examples of these are hydroxides, alkoxides or organometallic compounds.

Preferably, tin catalysts, titanium catalysts or lithium catalysts are used.

10 In the direct transesterification of the hemiacetal according to variant a), preferably dialkyltindicarboxylates are added as catalysts.

The amount of catalyst used is 0.001 to 20 mol%, preferably 0.005 to 5 mol%, and particularly 15 preferably 0.02 to 3 mol%.

The reaction mixture, in both variant a) and variant b), is preferably heated to the boiling point of the reaction mixture, so that the reaction temperature, depending on the reactants, is between 20 20°C and 200°C. The transesterification can be carried out further at atmospheric pressure, but also at reduced pressure or superatmospheric pressure from 0.001 to 200 bar. Preferably, the pressure is between 0.01 and 10 bar, particularly preferably it is 25 atmospheric pressure. The alcohol eliminated in the transesterification is preferably distilled off continuously.

If the alcohol used is a non-anhydrous alcohol, the reaction mixture is heated before the catalyst is 30 added, the water is distilled off and only then is the catalyst added.

Removal of the catalyst after the reaction ended succeeds in good yield by washing with water, hydrolyzing the catalyst and filtering the metal oxide 35 which precipitated out or, preferably by distilling off the product from the catalyst, preferably on a thin-film or short-path evaporator. It is also possible, in particular in the case of removal by distilling off the

product, to recycle the removed catalyst or the distillation residue to a new reaction mixture.

Subsequently to the transesterification reaction, the acetal cleavage is performed to give the free glyoxylic ester or its hydrate. The acetal cleavage is carried out by acid catalysis or in the presence of lanthanide catalysts. Suitable catalysts for the acid catalysis are acids in which the risk of hydrolyzing the ester moiety is as low as possible. Examples of these are H<sub>2</sub>SO<sub>4</sub>, p-toluenesulfonic acid, etc., and, in particular for variant b), formic acid, acetic acid, etc. Lanthanides which come into consideration are various compounds of cerium, lanthanum, ytterbium, samarium, etc. These are, in particular, chlorides, sulfates, carboxylates.

In the acetal cleavage, the free aldehyde groups of the glyoxylic ester are formed with elimination of the corresponding alcohol. The alcohol is preferably distilled off continuously in this case.

The preferred end product is the hydrate of the desired glyoxylic ester, so that the free glyoxylic ester is, if appropriate, converted into the hydrate by addition of water.

In a particular embodiment, the glyoxylic ester methyl hemiacetal or acetal is, after transesterification is complete, cleaved by means of formic acid. In this case, the reaction between the methanol being eliminated and the formic acid forms methyl formate and water. The methyl formate is separated off, and the reaction water forms directly the desired hydrate of the glyoxylic ester.

In a particularly preferred embodiment, the acetal of variant a) or b) is heated with formic acid for a short period, that is to say to the boiling point in less than one hour, the methyl formate is taken off and the remaining reaction mixture is rapidly cooled. This process variant is particularly advantageous in the preparation of the menthyl ester, since byproduct

formation, i.e. menthene formation, is avoided. Residual formic acid is extracted or preferably distilled off. The remaining reaction mixture is preferably dissolved in hexane either directly while 5 still warm or after heating.

The hexane solution is then washed with hot water and the end product is crystallized out from the organic phase.

The hexane mother liquor can be recycled and reused for 10 subsequent isolations without loss of quality to the end product.

Preferably, the desired end products are prepared by variant b).

By means of the inventive process, conversion 15 rates of up to 100% are achieved, the yields are above 95%, while according to the prior art (Tetrahedron), yields of only up to 80% are achieved. Owing to the mild transesterification conditions, product purities of greater than 99.9% up to 100% can be achieved.

DOCUMENTA DEPOSITA

Example 1:

a) Preparation of glyoxylic acid methyl ester dimethyl acetal

1200 g (10 mol) of glyoxylic acid methyl ester methyl hemiacetal and 40 g of concentrated sulfuric acid were heated to 105°C in a distillation apparatus consisting of a bottom vessel, stirrer, distillation column (10 plates) and distillation head with reflux divider. 300 g (9.4 mol) of methanol were pumped per hour through a spiral of a stainless steel tube which was thermostated to 110°C in a heating bath. The methanol vapor exiting at the outlet of the heating spiral was introduced into the reaction solution using a submerged tube at the bottom of the bottom-phase vessel. The reflux divider at the top of the distillation column was set to a ratio of take-off to reflux of approximately 10:1, as a result of which stationary conditions were rapidly established with a top temperature of approximately 70°C and a bottom temperature of 105°C. After 6 h the reaction was complete, the introduction of methanol vapor was stopped and the heating was shut off. The reaction mixture was then neutralized with solid sodium hydrogen carbonate. The apparatus was evacuated and the reaction mixture fractionally distilled. 1270 g (9.5 mol) of glyoxylic acid methyl ester dimethyl acetal having a content of 99.5% (GC) were obtained. The yield based on glyoxylic acid methyl ester methyl hemiacetal was thus 95%.

b) Transesterification of glyoxylic acid methyl ester dimethyl acetal to L-menthyl glyoxylate dimethyl acetal

402 g (3 mol) of glyoxylic acid methyl ester dimethyl acetal, 312 g (2 mol) of L-menthol and 1 g of dibutyltin diacetate were heated to 105°C in the apparatus described in step a). Methanol formed by the transesterification was taken off continuously at the top of the column. The reaction was complete after

15 h. The residual L-menthol content was < 0.1% (GC). The reaction mixture was freed from the catalyst in the short-path evaporator at 10 mbar, with approximately 15 g of catalyst solution being produced at the bottom 5 of the short-path evaporator, and 635 g of reaction mixture in the distillate of the short-path evaporator. The reaction mixture was then fractionally distilled under reduced pressure. 130 g (0.97 mol) of a glyoxylic acid methyl ester dimethyl acetal and 501 g (1.94 mol) 10 of L-menthyl glyoxylate dimethyl acetal having a content of 99% were obtained. The yield, based on glyoxylic acid methyl ester dimethyl acetal was 97% of theory.

The catalyst solution arising at the bottom of the 15 short-path evaporator was used in a new operation instead of the fresh dibutyltin diacetate. After carrying out the experiment using 402 g of glyoxylic acid methyl ester dimethyl acetal and 312 g of L-menthol as specified above, 509 g (1.95 mol) of 20 L-menthyl glyoxylate dimethyl acetal having a content of 99% were obtained. The yield, based on glyoxylic acid methyl ester dimethyl acetal, was therefore 98% of theory.

25 **c) Acetal cleavage of L-menthyl glyoxylate dimethyl acetal to give L-menthyl glyoxylate monohydrate**

100 g (0.39 mol) of L-menthyl glyoxylate dimethyl acetal and 400 g of formic acid were heated to boiling for 12 min in the apparatus described in step 30 a). Methyl formate was taken off at the top of the column, while formic acid was held in the reaction system at a bottom temperature of approximately 100°C. The reaction mixture was then rapidly cooled to room temperature, the apparatus was evacuated and the formic 35 acid was taken off. The residue was dissolved in 800 g of n-hexane by brief heating to boiling temperature. The hexane solution was washed twice, each time with 400 ml of water at 60°C. The hexane solution was then cooled, with L-menthyl glyoxylate monohydrate

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crystallizing out. The crystals were filtered off, the filter cake was washed with 100 g of cold hexane and dried at room temperature under reduced pressure. 64.6 g (0.28 mol) of L-menthyl glyoxylate monohydrate 5 having a purity of 99.8% (HPLC) were obtained. The angle of rotation ( $\alpha_D^{20} = -74^\circ$ , c = 1 g/100 ml, acetonitrile/water 95:5) and the FTIR spectra and <sup>1</sup>H-NMR spectra were in correspondence.

The mother liquor and the washing hexane were 10 combined, concentrated to 800 g and used in a new operation instead of the fresh n-hexane. After the experiment was carried out using 100 g of L-menthyl glyoxylate dimethyl acetal and 400 g of formic acid as specified above, 86.4 g (0.38 mol) of L-menthyl 15 glyoxylate monohydrate having a purity of 99.8% (HPLC) were obtained. The angle of rotation ( $\alpha_D^{20} = -74^\circ$ , c = 1 g/100 ml, acetonitrile/water 95:5) and the FTIR spectra and <sup>1</sup>H-NMR spectra were in correspondence. The yield was therefore 97% of theory.

DOCUMENTA DEPOSITA

## Claims

1. A process for preparing glyoxylic esters, which comprises
  - 5 a) transesterifying a glyoxylic ester hemiacetal directly with an alcohol in the presence of a catalyst, or
  - b) first converting a glyoxylic ester hemiacetal into the corresponding glyoxylic ester acetal and then
    - 10 transesterifying it with an alcohol in the presence of a catalyst,
- whereupon, following a) and b), the acetal is cleaved to give the desired free glyoxylic ester or its hydrate.
  - 15 2. The process as claimed in claim 1, wherein the glyoxylic acid ester hemiacetals used are glyoxylic acid methyl ester, ethyl ester, n-propyl ester, isopropyl ester, or t- or n-butyl ester hemiacetals.
  - 20 3. The process as claimed in claim 1, wherein the conversion to the complete acetal is performed using a liquid or vaporous alcohol selected from the group consisting of methanol, ethanol, propanol, butanol and hexanol in the presence of an acid as catalyst.
  - 25 4. The process as claimed in claim 1, wherein the transesterification is performed using a chiral or nonchiral, primary, secondary or tertiary alcohol.
  - 30 5. The process as claimed in claim 4, wherein the alcohol used is an acyclic, monocyclic, bicyclic terpene alcohol, an acyclic, monocyclic or tricyclic sesquiterpene alcohol, di- or triterpene alcohol.
  - 35

6. The process as claimed in claim 1, wherein the catalyst used is a stannic ester, titanic ester or zirconic ester, a lithium compound or, the basic catalyst used is an alkali metal compound,  
5       alkaline earth metal compound or aluminum compound.

7. The process as claimed in claim 6, wherein the catalyst used is dialkyltin dicarboxylate having  
10      1-12 carbon atoms in the alkyl moiety, titanium(IV)ethoxide, titanium(IV) isopropoxide, titanium(IV) n-propoxide, titanium(IV) n-butoxide or titanium(IV) isobutoxide, or butyllithium.

15 8. The process as claimed in claim 1, wherein the acetal is cleaved by acid catalysis in the presence of  $H_2SO_4$ , p-toluenesulfonic acid, formic acid or acetic acid, or in the presence of a lanthanide catalyst.  
20

9. The process as claimed in claim 8, wherein the acetal is cleaved by brief heating of the acetal for up to 1 hour up to boiling point with formic acid, removal of the formate formed and rapid cooling, whereupon the product is crystallized out of a diluent, if appropriate after previous extraction of impurities with water, and isolated.  
25

SEARCHED  
INDEXED  
MAILED  
FILED

## DECLARATION AND POWER OF ATTORNEY FOR U.S. PATENT APPLICATION

( ) Original      ( ) Supplemental      ( ) Substitute      ( PCT)      ( ) Design

As a below named inventor, I hereby declare that: my residence, post office address and citizenship are as stated below next to my name; that I verily believe that I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural inventors are named below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

Title: Process for preparing glyoxylic esters or their hydrates

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of which is described and claimed in:

( ) the attached specification, or  
 ( ) the specification in the application Serial No. \_\_\_\_\_ filed \_\_\_\_\_;  
 and with amendments through \_\_\_\_\_ (if applicable), or  
 (  ) the specification in International Application No. PCT/ EP99/09517, filed 06/12/1999, and as amended  
 on \_\_\_\_\_ (if applicable).

I hereby state that I have reviewed and understand the content of the above-identified specification, including the claims, as amended by any amendment(s) referred to above.

I acknowledge my duty to disclose to the Patent and Trademark Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.

I hereby claim priority benefits under Title 35, United States Code, §119 (and §172 if this application is for a Design) of any application(s) for patent or inventor's certificate listed below and have also identified below any application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

COUNTRY	APPLICATION NO.	DATE OF FILING	PRIORITY CLAIMED
Austria	A2173/98	28.12.1998	yes

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose information material to patentability as defined in Title 37, Code of Federal Regulations, §1.56 which occurred between the filing date of the prior application and the national or PCT international filing date of this application.

APPLICATION SERIAL NO.	U.S. FILING DATE	STATUS: PATENTED, PENDING, ABANDONED

And I hereby appoint John T. Miller, Reg. No. 21,120; Michael R. Davis, Reg. No. 25,134; Matthew M. Jacob, Reg. No. 25,154; Jeffrey Nolton, Reg. No. 25,408; Warren M. Cheek, Jr., Reg. No. 33,367; Nils E. Pedersen, Reg. No. 33,145 and Charles R. Watts, Reg. No. 33,142, who together constitute the firm of WENDEROTH, LIND & PONACK, L.L.P., attorneys to prosecute this application and to transact all business in the U.S. Patent and Trademark Office connected therewith.

I hereby authorize the U.S. attorneys named herein to accept and follow instructions from Patent Department; DSM Fine Chemicals Austria Nfg GmbH & Co KG my action to be taken in the U.S. Patent and Trademark Office regarding this application without direct communication between the U.S. attorneys and myself. In the event of a change in the persons from whom instructions may be taken, the U.S. attorneys named herein will be so notified by me.

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I further declare that all statements made herein of my own knowledge are true, and that all statements on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

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 6th Inventor \_\_\_\_\_ Date \_\_\_\_\_  
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The above application may be more particularly identified as follows:

U.S. Application Serial No. \_\_\_\_\_ Filing Date \_\_\_\_\_  
 Applicant Reference Number \_\_\_\_\_ Atty Docket No. \_\_\_\_\_  
 Title of Invention \_\_\_\_\_